IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: **WAVE 4 CASES LISTED IN MOTION EXHIBIT A**	

DEFENDANTS' REPLY IN SUPPORT OF MOTION TO LIMIT THE TESTIMONY OF PROF. DR. MED. UWE KLINGE

Defendants Ethicon, Inc., Ethicon, LLC, and Johnson & Johnson (collectively, "Ethicon") submit this Reply in Support of their Motion to Exclude the Opinions and Testimony Prof. Dr. Med. Uwe Klinge [Doc. [3626] ("Motion")] and Memorandum of Law in Support [Doc. [3630] ("Mem.")]. Ethicon requests that the Court grant its Motion and reject the arguments raised in Plaintiffs' Response to the Motion [Doc. [3767] ("Response")].

ARGUMENT

I. Dr. Klinge should not be permitted to testify about alternative designs to Prolene in Ethicon's SUI products.

Dr. Klinge cannot identify any scientific testing or literature that shows that Ethicon's SUI products would be **both** safer **and** equally effective if it were made of Ultrapro or PVDF. Because there is no such testing or literature, his opinions on alternative designs should be excluded. *Nease v. Ford Motor Co.*, 848 F.3d 219 (4th Cir. 2017).

A. Expert opinions regarding alternative designs must be supported by testing or scientific literature demonstrating that he proposed alternative is actually safer and equally or more effective.

As the Fourth Circuit recognized in *Nease*, an "especially important factor for guiding a court in its reliability determination is whether a given theory has been tested." *Nease*, 848 F.3d at 231. In *Nease*, the Fourth Circuit discusses and highlights the importance of scientific testing to establish the reliability of an expert's methodology and resulting opinions. As the Fourth Circuit has repeatedly recognized, "[A] plaintiff may not prevail in a products liability case by relying on the opinion of an expert unsupported by any evidence such as test data or relevant literature in the field." *Id*. (quoting *Oglesby v. Gen. Motors Corp.*, 190 F.3d 244, 249 (4th Cir. 1999)). *See also Conklin v. Novartis Pharmaceuticals Corp*., 2012 WL 4127295, *10 (E.D. Tex. Sept. 18, 2012) (rejecting alternative design where expert failed to show that lower dose of drug would effectively fight the plaintiff's cancer).

Plaintiffs apparently do not dispute that Dr. Klinge has not conducted any clinical or scientific testing evaluating both the safety and efficacy of SUI or POP devices constructed with his proposed alternative materials as compared to Ethicon's SUI or POP devices. Pls.' Opp. at 6-8. He has not made an Ethicon device out of any alternative material and tested it, not even in a cadaver. Nor has anyone else.

Instead, he offers inapposite speculation about two materials, Ultrapro and PVDF.

B. Ultrapro

Plaintiffs' claim that a mesh like Ultrapro—which has some absorbable fibers—would work in a device to treat SUI is inherently speculative. When Ethicon tried to make a device out of a mesh like Ultrapro, TVTO-PA, the FDA refused in 2011 to allow it to be marketed because there was inadequate evidence to support the safety and effectiveness necessary for clearance.

When the device flunked Ethicon's cadaver tests, it ended the project. Plaintiffs' experts have many theories about why a larger pore mesh might be safer, but they have no evidence that it would be effective. In fact, the Prolene mesh Ethicon already uses has a pore size larger than that of all other incontinence devices.

Plaintiffs contend that Dr. Klinge has a reliable basis for his opinion that Ultrapro mesh is a safer alternative design, citing as support a 2013 journal article by Okulu about a single experiment in Turkey. Mot. Ex. D, Okulu et al., *Use of three types of synthetic mesh material in sling surgery: A prospective randomized clinical trial evaluating effectiveness and complications*, 47 SCANDINAVIAN J. UROLOGY 217, 223 (2013). But the Okulu article—which is the only source Dr. Klinge has identified to support his opinion that Ultrapro might actually be effective in treating stress urinary incontinence—involved a different surgical procedure and did not include any Ethicon devices as a comparator. It discusses an alternative surgery, not an alternative design for an Ethicon device.

The authors of that study employed a different surgical technique described as a "double-forced sling." *See* Okulu et al., *supra*. at 217–224. The Okulu surgery cut open the vagina and did not use trocars. The surgeons sutured a small mesh patch to fascia in the abdomen, and did not leave it tension-free. The surgery was different, the method of implantation was different, and the operation, unlike the TVT devices, required a general anesthetic and overnight stay in the hospital. In short, the study cited involves a completely different surgical procedure and so falls within this Court's rulings that it will not allow expert testimony about different surgical procedures because they do not constitute alternative designs for a device. *In re Ethicon, Inc.*, 2017 WL 1264620 (S.D. W.Va. March 29, 2017 at *3 (excluding expert testimony of alternate surgical procedures).

Furthermore, the authors of the Okulu study expressly disclaimed any comparison to Ethicon devices and the type of surgery they require. The authors acknowledged that "[t]his surgical method also *needs evaluation,* especially in comparison with the traditional TVT sling procedure." *Id.* at 223 (emphasis added). Because the study did not involve the same surgical technique as the sling devices manufactured by Ethicon, Dr. Klinge cannot rely on that study as support for his opinion that Ethicon's devices would be safer if Ethicon used Ultrapro rather than Prolene mesh. *Mullins v. Ethicon, Inc.*, 2:12-cv-02952, at 3-5 (S.D. W. Va. Feb. 23, 2017) (explaining that alternative surgeries and procedures are not alternative designs because they "do not inform the jury on *how* the [device's] design could have feasibly been made safer to eliminate the risks that caused the plaintiff's injuries.").

Dr. Klinge admitted as much in deposition, testifying that he believes Ultrapro is safe and effective when used in the manner described in the Okulu article, but not if it were to be used in the same manner Prolene mesh is used in Ethicon's devices, i.e. as a sling, or "ligament":

> That the treatment has to be – you have to differentiate in what form you want to have it. If you're using the ULTRAPRO to – to serve as a ligament, as the PROLENE is intended to use, then you have the problem of the pore collapse. So the large-pore ULTRAPRO becomes a small-pore mesh device with all the risks.
>
> If you use it like the Turkish people [i.e., the authors of the Okulu study], and in fact at that time point I didn't have the idea that someone is using it in a different way. If you are using it to reinforce the tissues, as we did it with the flat meshes, then you don't have the risk for pore collapse, as with the ligaments, and with this procedure maybe it is a good idea to have it. *But to use it as a ligament it's not a good idea, and as a ligament I don't want to have it.*

Mot. Ex. E, Klinge 11/4/15 Dep. Tr. 285:5–20 (emphasis added). And his opinion as to "safety" simply ignores the more extensive anesthesia, surgery, and hospital stay the patients in the Okulu study had to endure. Additionally, although TVT has long-term data supporting its safety and efficacy, *see* Reply Ex. I, C. G. Nilsson et al., *Seventeen Years' Follow-up of the Tension-free*

Vaginal Tape Procedure for Female Stress Urinary Incontinence, 2013 THE INT'L UROGYNECOLOGICAL ASS'N (2013), the Okulu study, reporting the results over a 4-year period, does not demonstrate equal or greater long-term safety and efficacy.

In short, Okulu, which did not involve a TVT device, does not stand for the proposition that Ultrapro, when employed like the Prolene mesh in Ethicon's TVT devices, is safe and effective at treating stress urinary incontinence. As a result, Dr. Klinge is "not able to predict" whether "in the specific function of a sling the Ultrapro really over the time will work really better or whether it will create some new problems." Mot. Ex. F, Klinge 10/5/15 Dep. Tr. 92:17–93:4. Because Dr. Klinge has not tested his hypothesis or cited to any peer-reviewed study that actually compares his proposed alternatives with Ethicon's mesh devices *and* corresponding surgical procedures, his opinions are speculative and should be excluded. *Nease*, 848 F.3d at 231-232.

Finally, Plaintiffs ask the Court to disregard Dr. Klinge's prior testimony that Ultrapro is subject to the same criticisms he levies against Prolene, claiming that Dr. Klinge, in his report, "spends pages and pages explaining the basis for his opinion . . . that lighter-weight, larger-pore mesh like Ultrapro is safer than Prolene." Pls.' Opp. at 9.

But Dr. Klinge has repeatedly and steadfastly testified that Ultrapro is neither safe nor effective at treating stress urinary incontinence when implanted in the same manner as Prolene mesh in TVT. *See id.* (testifying that using Ultrapro the way Prolene mesh is intended to be used is "not a good idea" because it "becomes a small-pore mesh device with all the risks"); *see also* Mot. Ex. G, Klinge 11/15/13 Dep. Tr. 529:12–23 (testifying that Ultrapro "is not sufficient to withstand—or to preserve the big pores—under these conditions of biomechanics as it is required for the use as a sling"). The jury should not be permitted to hear testimony Dr. Klinge

has admitted for years is untrue.

C. PVDF

Again, Dr. Klinge's opinion that PVDF mesh is a feasible alternative design is not supported by clinical testing or scientific literature demonstrating that an Ethicon device made using PVDF mesh—which incorporates extremely small pores—would in fact be safer and equally effective in treating incontinence. No other American device manufacturer uses it to treat incontinence.

Yet, Plaintiffs argue that Dr. Klinge's opinions regarding PVDF are reliable and admissible. Plaintiffs spend approximately one page of their response arguing that PVDF is a safer alternative because it is purportedly associated with a lower incidence of a select number of potential complications, Pls.' Opp. at 11, and another page arguing that PVDF was a feasible alternative to the mesh used in Ethicon's mesh devices because the material was previously available to Ethicon. Pls.' Opp. at 12.[1]

However, neither Dr. Klinge nor Plaintiffs identify reliable testing comparing the safety ***and*** efficacy of an Ethicon sling constructed with PVDF and any of Ethicon's mesh devices for the treatment of SUI, nor do they identify any reliable medical literature documenting the results of any such testing. Additionally, the mere existence and availability of PVDF mesh is "wholly insufficient to prove that [it was] safer" in the context of treating stress urinary incontinence, or

[1] Although Dr. Klinge attempts to provide support for his opinion that PVDF is a safer alternative to Prolene for the treatment of SUI, Plaintiffs cannot overcome the fact that Dr. Klinge has never examined whether PVDF is subject to the same deficiencies he identifies in Prolene. *See* Mot. Ex. F, Klinge 10/5/15 Dep. Tr. 95:15-24 (testifying he does not know whether PVDF is subject to particle loss).

that a "reasonably prudent manufacturer[] would have adopted" it for use in mid-urethral slings. *Nease*, 848 F.3d at 334.

As such, the Court should exclude Dr. Klinge's opinions regarding alternative designs.

II. The Court Should Limit Certain of Dr. Klinge's Opinions Regarding Prolene Soft Mesh Used in Ethicon's Prolapse Products.

A. The Court should exclude any testimony from Dr. Klinge regarding alternative designs to Prolene Soft for use in treating prolapse.

Plaintiffs argue that Dr. Klinge's opinions regarding alternative designs to Prolene Soft are reliable and admissible, based upon this Court's ruling in *In re Ethicon, Inc.*, No. 2:12-md-2327, 2016 WL 4473446, at *2 (S.D. W. Va. Aug. 24, 2016) (hereinafter "*Wave 1* Order"), which cited as support its order in *Lewis*. Pls.' Opp. at 14. However, the Court's *Wave 1* Order did not distinguish between Dr. Klinge's Prolapse Report and his SUI Report. That distinction is significant.

As discussed above, Dr. Klinge's opinions regarding PVDF as an alternative design to Ethicon mesh products used to treat SUI are unreliable because the literature on which he relies does not show that PVDF is both safer and at least as effective as Ethicon mesh products. Conversely, Dr. Klinge made no such effort in his Prolapse Report. Indeed, Dr. Klinge failed to identify even a single study to support his opinion that PVDF mesh—a stiff, small-pore mesh that does not stretch—is a feasible alternative for treatment of POP.

To be clear, the *only* time Dr. Klinge references PVDF in his entire Prolapse Report is page 16, where he states, "The PVDF product, Dynamesh, is a safer design than Gynemesh PS [i.e., Prolene Soft Mesh] for all of the reasons stated above as further established in Muehl's testing." Mot. Ex. C, Klinge Prolapse Report at 16. Yet Dr. Klinge does not identify, in the body of his Prolapse Report, *any* reason why mesh made of PVDF is supposedly not only safer than

Ethicon's chosen mesh but also equally effective. If ever there was *ipse dixit* by an expert witness, this is it.

Not only are the reasons for Dr. Klinge's opinion absent, so too is any supporting literature. Plaintiffs claim that "Dr. Klinge references numerous peer-reviewed articles that support his opinions regarding PVDF as an alternative design to the Gynemesh PS used in the Prolift devices." Pls.' Opp. at 14. But nowhere in the actual Prolapse Report does Dr. Klinge reference any literature supporting his statement that PVDF is safer **and** equally or more effective than polypropylene for treatment of prolapse. The articles Plaintiffs cite appear only in his *curriculum vitae* with no explanation as to how, if at all, they support his opinion.

Because of the differences between his SUI Report and Prolapse Report, this Court's ruling in *Lewis*—which examined the reliability of Dr. Klinge's opinions regarding alternatives for treatment of SUI—is inapposite.

Instead, the Court should be guided by its ruling in *Bellew*, rendered after *Lewis* in a case involving a prolapse product and a report by Dr. Klinge that was identical to his current Prolapse Report. *See* Mem. Op. & Order [Doc. 265] at 16-17, *Bellew v. Ethicon, Inc.*, No. 2:13-cv-22473 (S.D. W. Va. Nov. 20, 2014).

The Court in *Bellew* precluded Dr. Klinge from testifying about safer alternatives due to his failure to cite to peer-reviewed studies supporting his opinions, and because he provided "no indication that his alternative design opinions are based on anything other than his and Dr. Mühl's effective porosity testing and internal Ethicon documents," which were "not sufficiently reliable scientific bases" to pass scrutiny under *Daubert*. the Court precluded him from testifying about safer alternatives. *Id.*

Dr. Klinge's testimony in *Bellew* demonstrates that the Court was correct to preclude him

from offering opinions on safer alternatives. Specifically, Dr. Klinge conceded that he is not aware of any peer-reviewed studies supporting his opinion that PVDF is safer and equally or more effective than Ethicon's POP devices for the treatment of POP. Mot. Ex. H, Klinge 11/10/14 Dep. 182:14-184:4. Indeed, he testified that he could not identify a single mesh with an acceptable risk/benefit profile for the treatment of POP. *Id*. at 184:3-6.

Dr. Klinge's Prolapse Report is identical to the report at issue in *Bellew*. The Court should again preclude Dr. Klinge from testifying about alternative designs to Ethicon's prolapse products. In short, nowhere in his Rule 26 expert report or in his *de bene esse* deposition does Dr. Klinge cite any peer-reviewed literature that demonstrates that PVDF or a mesh with larger pores would actually be safer alternatives to Prolene Soft, much less equally effective alternatives. Instead, he cites to certain studies in his CV—with no discussion or analysis in the body of his report—and otherwise relies only on his "effective porosity testing and internal Ethicon documents, which are not sufficiently reliable scientific bases under *Daubert*." *Bellew* Order at 16. As a result, he should not be permitted to testify regarding alternative design in cases involving Ethicon's prolapse products. *See Nease*, 848 F.3d at 234.

B. The Court should exclude Dr. Klinge's opinions regarding fraying and particle loss in Prolene Soft.

Plaintiffs do not dispute that the Prolene Mesh in Ethicon's TVT family of products and the Prolene Soft Mesh in its pelvic organ prolapse products have different designs, including different pore sizes and different weights. Plaintiffs also ignore a key distinction in the manufacturing process: whereas Prolene Mesh can be cut mechanically, Prolene Soft is cut ultrasonically.

Because of these distinctions, Dr. Klinge's reliance on internal company documents relating to the TVT—a midurethral sling that uses Prolene Mesh rather than Prolene Soft—and a

2003 study about the TVT do not support his opinion that Prolene Soft frays and loses particles.

Dr. Klinge is making an unfounded assumption that what happens to the Prolene mesh in TVT must also happen to the Prolene Soft mesh in Ethicon's prolapse products. However, insofar as these TVT-related materials are the only materials Dr. Klinge cites in his report, he should be precluded from testifying at trial about Prolene Soft mesh fraying or losing particles.

Recognizing the shortcomings in Dr. Klinge's report, Plaintiffs in their response cite as additional support a peer-reviewed article by Dr. Klinge and colleagues that is referenced in his Prolapse Report and one page of what appears to be a PowerPoint slide referencing the same study by Dr. Klinge. Neither Plaintiffs nor Dr. Klinge explain, however, how this study—which concerns elongation of under load—supports his opinion that Prolene Soft Mesh is subject to fraying and particle loss. Plaintiffs bear the burden of "com[ing] forward with evidence from which the court can determine that the proffered testimony is properly admissible." *Tyree v. Boston Scientific Corp.*, 54 F. Supp. 3d 501, 516 (S.D. W. Va. 2014). Surely they cannot satisfy that burden simply by citing, without any explanation, a single article that does not speak to the issue.

CONCLUSION

WHEREFORE, FOR THESE REASONS and as more fully set forth in Ethicon's motion and supporting memorandum of law, Ethicon respectfully requests that this Court enter an order granting its Motion to Limit the Testimony of Prof. Dr. Med. Uwe Klinge.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that on May 4, 2017, I electronically filed this document with the clerk of the court using the CM/ECF system, which will send notification of this filing to CM/ECF participants registered to receive service in this MDL.

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